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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SUTHERLAND ASBILL & BRENNAN LLP
999 PEACHTREE STREET, N.E.
ATLANTA, GA 30309

EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/801,221	SANBERG ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *87-123* is/are pending in the application.

4a) Of the above claim(s) *112-123* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *87-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 28, 2004 has been entered. Claims 4-20, 43-61, and 70-86 have been cancelled. Claims 87-123 have been newly added.

Claims 112-123 are directed to non-elected inventions. See the restriction requirement mailed July 11, 2002. The elected invention is directed to neural cells, a method of producing neural cells, and cell compositions.

Claims 112-123 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in the reply filed on September 5, 2002.

Accordingly, Claims 87-111 are examined herein.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 28, 2004 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 87-111 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 2-3 of the Office Action mailed 11/26/02, on pages 3-4 of the Office Action mailed 1/2/04, and for further reasons as discussed herein, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to methods of producing neural cells and cell compositions.

The specification fails to provide an enabling disclosure for the claimed compositions and methods of making said compositions because methods of transplantation of neural tissue or other cells into the CNS or PNS are not routinely successful and the specification does not offer adequate guidance to enable one skilled in the art to practice the claimed invention to derive a therapeutic benefit in a diseased animal. The specification teaches that the only use for the claimed compositions is for transplantation to produce a therapeutic effect but the specification does not adequately teach how to use the claimed method to produce such an effect. Jackowski et al. (1995) details the limitations and unpredictability associated with the transplantation of neural tissue. At page 311, column 1, paragraph 2, the reference discusses the barriers to successful transplantation of neural tissue, notably the presence of molecules that actively inhibit the regeneration of mammalian CNS and PNS axons. The specification does not offer any guidance as to how the claimed compositions could be used therapeutically for the treatment of any disorder, including Parkinson's disease (PD), Alzheimer's disease (AD), Huntington's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Tay Sach's disease, Rett Syndrome, lysosomal storage disease, ischemia, spinal cord damage, ataxia, schizophrenia, or autism, as contemplated in the specification. While the specification discloses the use of human cord blood fractions that have been used either directly upon thawing (cord blood mononuclear cells) or treated in culture for a week with various trophic factors (BDNF, NGF, EGF+bFGF) prior to transplantation into a rat stroke

model (pages 58-65), the claims cover the preparation of a great variety of cell compositions, including terminally-differentiated cells, which the specification does not teach how to use. The human cord blood fractions used directly upon thawing are not the cells produced by the claimed methods, but rather appear to be the starting material for use in the claimed method. With regard to the cells that were cultured with various trophic factors, the specification does not disclose the phenotype of these cells and the claims require the production of cells that exhibit an increase in the expression of genes associated with neurogenesis. The specification provides general teachings only (see pages 1-8 of specification), but does not provide specific guidance for treating a pathological condition. The specification fails to provide specific guidance for using the great variety of cell compositions covered by the claims, to provide a therapeutic benefit for the treatment of a disease or disorder.

Given the lack of applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the wide variety of cell types and cell compositions that could be produced using the claimed methods, and the unpredictability for using the cell compositions produced to achieve a therapeutic effect upon transplantation as asserted in the specification, one of skill in the art would have been required to engage in undue experimentation to make and use the claimed compositions.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

Applicants have not offered any arguments explaining how the present claims overcome the enablement rejection of record.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 87-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 87-111 are indefinite in their recitation of "increase" and "decrease" because it is unclear what would be considered the reference state for said "increase" or said "decrease". The claims now recite that the cell of interest should be compared to an "umbilical cord blood cell that has not been cultured in the presence of a differentiation agent" but the term "umbilical cord blood cell" covers a variety of different cell types, given that "umbilical cord blood" refers to a heterogeneous population of cells. Thus, it is unclear which cell type should be used as the reference cell. Is it the progenitor cell itself (i.e., the cell that gives rise to the cell of interest)? In the absence of recitation of some reference state or process for comparison said "increase" and said "decrease" remain indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 99-111 are rejected under 35 U.S.C. 102(a) as being anticipated by Kopen et al. (1999).

Claims 99-111 are directed to a composition comprising an isolated, differentiated, mononuclear cell from human umbilical cord blood, wherein the cell is isolated by a method comprising (a) obtaining a sample of mononuclear cells from the umbilical cord blood, and (b) growing the mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to differentiate the mononuclear cells, wherein the cell exhibits both an increase in the expression of genes associated with neurogenesis and a decrease in the expression of genes associated with hematopoiesis in comparison to an umbilical cord blood cell that has not been cultured in the presence of the differentiation agent.

Claims 99-111 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed compositions from any other composition comprising a neural cell. The claims only require that the cell must express genes associated with neurogenesis, while exhibiting a decrease in the expression of genes associated with hematopoiesis.

Kopen et al. (1999) disclose that marrow stromal cells (MSCs, also mesenchymal stem cells) injected into the lateral ventricle of neonatal mice differentiated into astrocytes and neurons. Since mesenchymal stem cells are also present in the mononuclear cell fraction of umbilical cord blood, the cells disclosed by Kopen et al. meet all the claim limitations.

Thus, the claimed compositions are disclosed in the prior art.

Applicants have not offered any arguments explaining how the claimed compositions are free of the art of record.

Claims 99-111 are rejected under 35 U.S.C. 102(b) as being anticipated by Reynolds et al. (1992).

The claims encompass terminally differentiated neural cells as well as a variety of neural progenitor cells known in the art.

Claims 99-111 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed compositions from any other composition comprising a neural cell. The claims only require that

the cell must express genes associated with neurogenesis, while exhibiting a decrease in the expression of genes associated with hematopoiesis.

Reynolds et al. (1992) disclose neurons, astrocytes, and neuroepithelial stem cells. All three cell types qualify as the cell type recited in the instant claims.

Thus, the claimed compositions are disclosed in the prior art.

Applicants have not offered any arguments explaining how the claimed compositions are free of the art of record.

Claims 99-111 are rejected under 35 U.S.C. 102(b) as being anticipated by Azizi et al. (1998).

The claims encompass cells derived from mesenchymal stem cells (MSCs), particularly cells produced when MSCs are induced to differentiate into neural cells upon contact with neural cells.

Claims 99-111 are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See MPEP 2113. Thus, the claims read on neural cells disclosed in the prior art, as discussed below. There are no structural limitations to distinguish the claimed compositions from any other composition comprising a neural cell. The claims only require that the cell must express genes associated with neurogenesis, while exhibiting a decrease in the expression of genes associated with hematopoiesis.

Azizi et al. (1998) disclose human marrow stromal cells (MSCs). They also examined the effects of direct injection of human MSCs into the brains of rats and found that the cells migrated from the injection site along known pathways for migration of neural stem cells to successive layers of the brain. Since mesenchymal stem cells are also present in the mononuclear fraction of umbilical cord blood, the cells disclosed by Azizi et al. meet all the claim limitations.

Thus, the claimed compositions are disclosed in the prior art.

Applicants have not offered any arguments explaining how the claimed compositions are free of the art of record.

Conclusion

No claims are allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic

Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER